



# Advanced lab and clinical cases: Finding new targets

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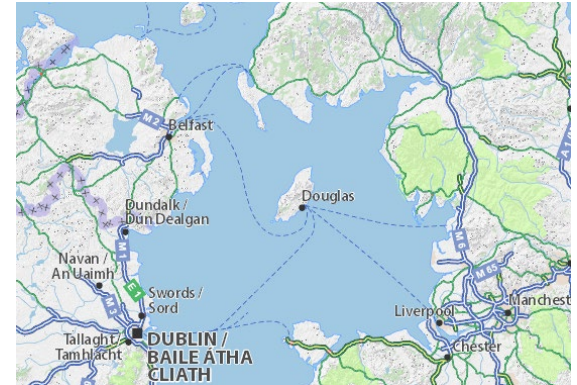
Royal Liverpool University Hospital

# Call from Noble's Hospital, IOM

40M presenting with anaemia and jaundice  
Being treated for haemolysis

PMH:

- AIHA diagnosed in late 20s
  - Last episode 9 years ago, splenectomy in Russia
  - Also episodes of ITP, Evans
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- No PMH/FH of autoimmune conditions
  - No clear trigger for this acute episode
  - No recent blood transfusions



# Investigations:

Hb	64 g/L	Reticulocytes	51 x10 <sup>9</sup> /L
MCV	98.8 fL	Haptoglobins	<0.1 g/L
Platelets	349 x10 <sup>9</sup> /L	LDH	503 I/L
WCC	44.1 x10 <sup>9</sup> /L	Bili	25 U/L
Neutrophils	37.4 x10 <sup>9</sup> /L	DAT	+++
Film- polychromasia, spherocytes, left shifted neutrophils		B12/folate	Normal

So far received:

- IVIg 2x 1g/kg
- Methylprednisolone – 2x 1g IV
- Rituximab 375mg/kg

# Transfused and sent on flight

- On arrival- feels pretty well, observations stable

## Suspecting AIHA

- Management:
  - Change to prednisolone
  - Complete 4x weekly doses of rituximab
  - Folic acid
  - LMWH prophylaxis
  - PPI, vit D & Ca supplements





# 2 days into admission...

- MET call: HR 145, confused, temp 39.2
- Darker urine
- ?bone pain in legs
- ECG shows ischaemic changes

Hb	26 g/L
Bili	98 umol/L
LDH	913

## **Acutely decompensated haemolysis and T2 MI**

- Call to transfusion lab- unable to confirm group so no blood available, awaiting further tests in the RCI lab
- Started on broad spectrum antibiotics
- Further IV methylprednisolone 1g
- Further IVIg 1g/kg

# Do you transfuse?

1. No, supportive measures only, i.e. fluids & O<sub>2</sub>
2. Transfuse suitable blood from RCI lab when available
3. Transfuse O neg

- *“If anaemia is life threatening in the time required for full compatibility testing, transfuse with ABO, Rh and K matched red cells”*

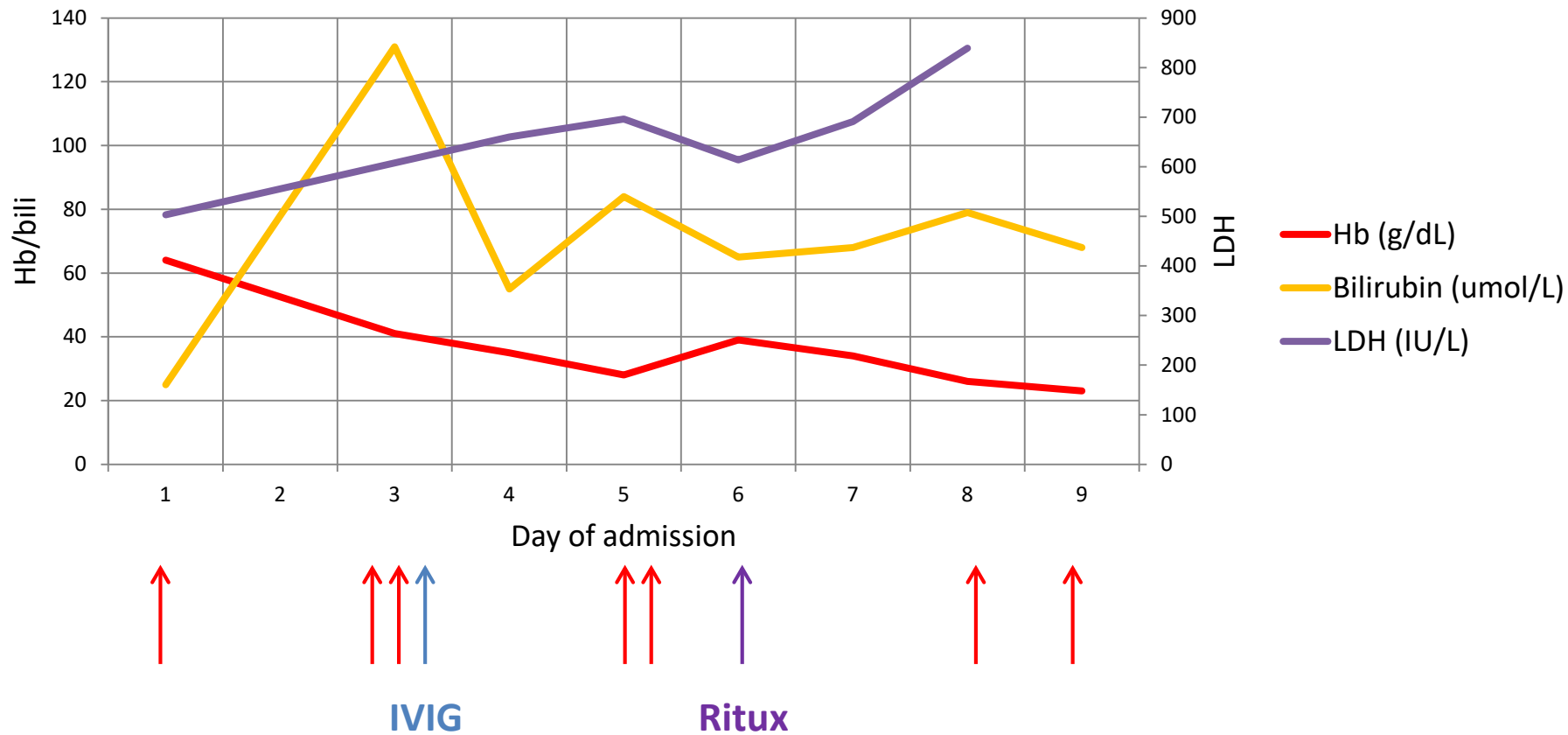
Hill et al. BSH guidelines. 2016

- Transfused 1 unit of O neg and a further unit from RCI when available

# In the RCI lab

- Auto panreactive, non-specified antibody detected by IAT
- No underlying alloantibodies identified in modified plasma
- Monospecific anti-IgG DAT +ve (C3 -ve)
- Genotyping in Sheffield awaited

Moved to ITU

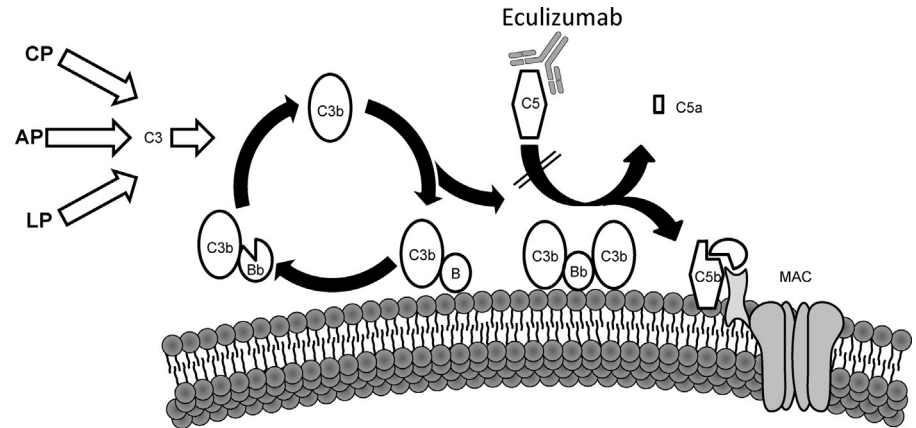


# What further treatment would you give?

1. Plasma exchange
2. Continue to transfuse as needed
3. Splenectomy
4. Proceed to further immunosuppression- azathioprine, ciclosporin, MMF
5. Complement inhibitor

# Eculizumab (Soliris)

- Humanised monoclonal IgG which binds with C5
- Targets terminal complement and MAC formation
- Licensed for PNH and aHUS
- Phase II trial in CAD – reduced transfusion requirements, ?reduce VTE
- Case reports of use in wAIHA



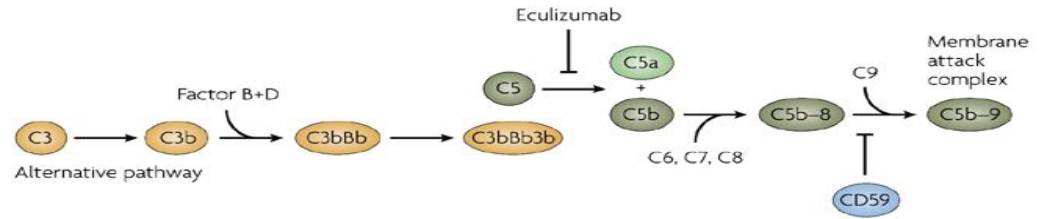
Röth et al. Blood, 2015.

Diagram: Wong et al. Molecular

Immunology, 2013

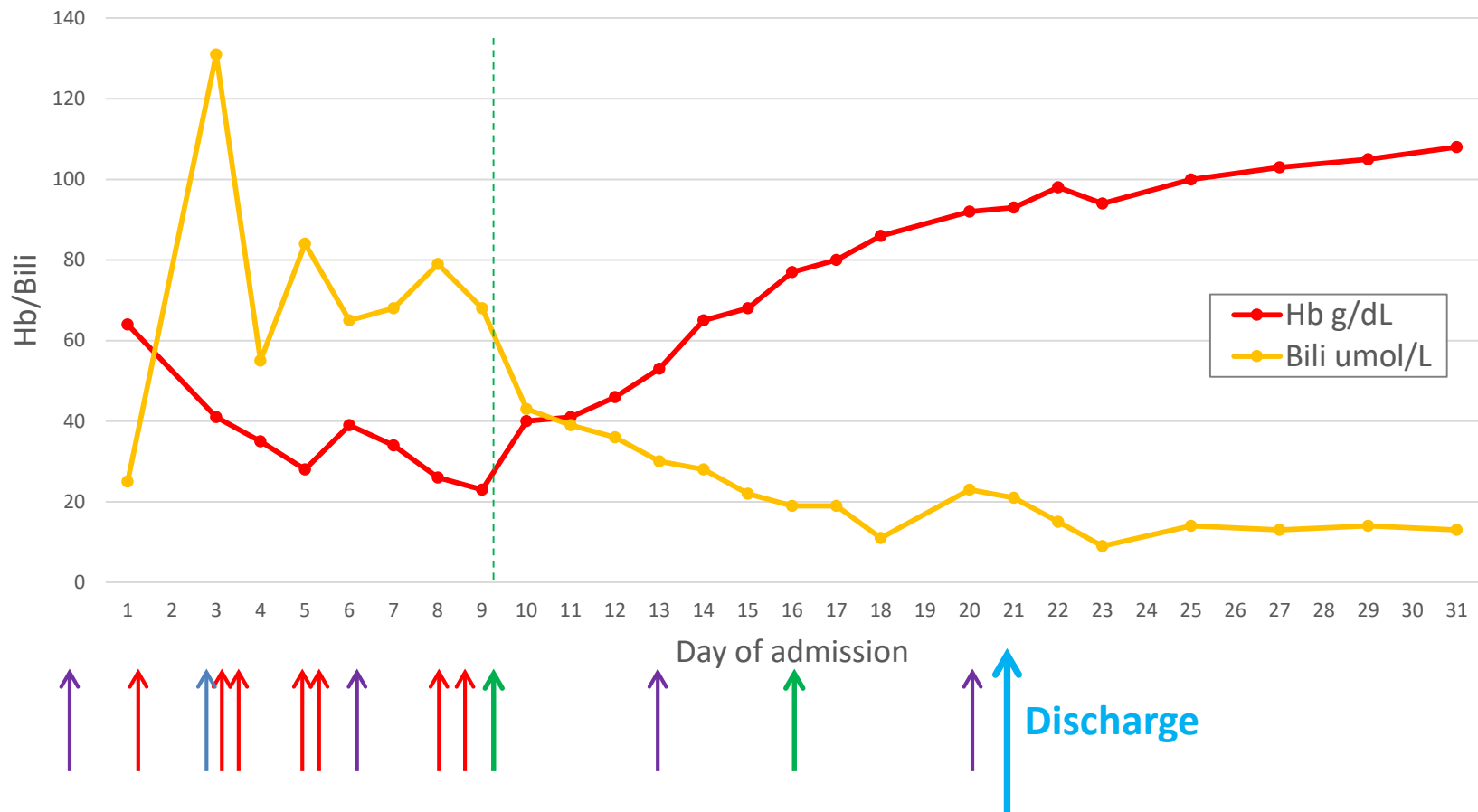
- Limitations:

- Holding measure
- No effect of extravascular haemolysis
- Relies on complement activation
- Risk of serious side effects, *Neisseria meningitidis* infection



# Eculizumab

- Not licensed
  - IFR submitted to IOM Health Services
  - Local pharmacy approval gained
- Given to patient on day 9



# Supportive treatment

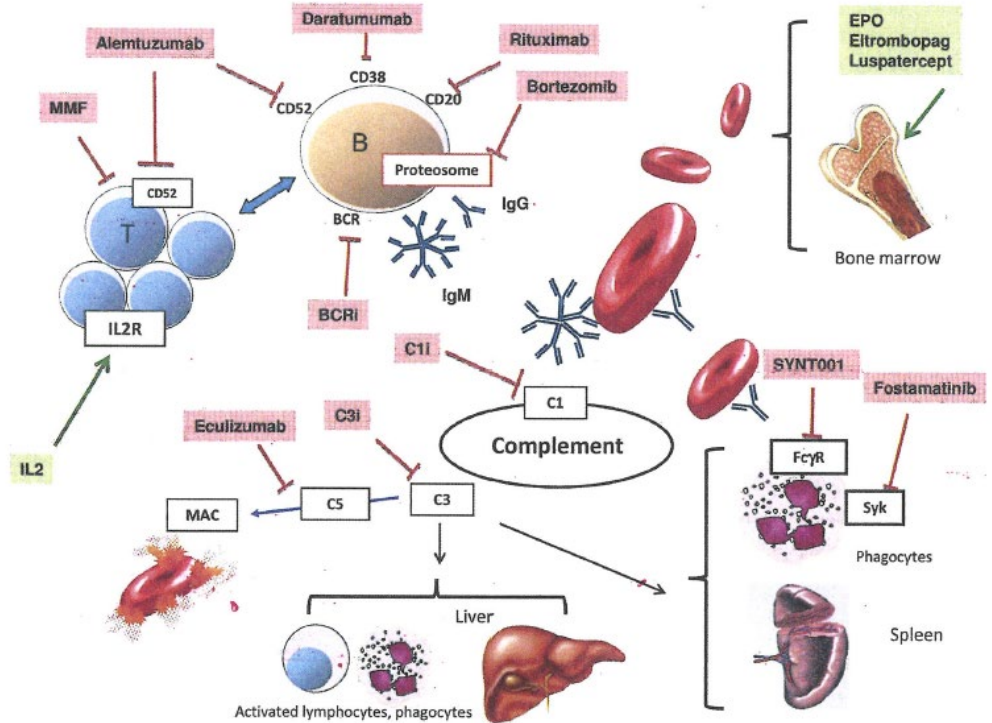
- Eculizumab
  - Men ACWY & B, if unable to do >2 weeks prior must cover with prophylactic antibiotics
- Splenectomy
  - Post splenectomy regimen – pneumovax, Hib
  - Penicillin V
- Steroids, rituximab
  - Septrin

# Underlying cause?

- CT TAP NAD, small lymph nodes
- BM NAD
- Parvovirus IgG/IgM neg
- Serum electrophoresis NAD
- PNH screen neg
- ANA/dsDNA neg
- Quantiferon- TB neg

# Going forward

- BCR inhibitors
- Proteasome inhibitors
- Complement
  - APL-2** C3 inhibition
  - Sutimlimab** C1s inhibition
  - ANX005** C1q inhibition
- Cellular immunity
  - Fostamatinib** syk inhibition
  - SYNT001** blocks FcRn and IgG interaction



# Points to learn from

1. Liaise early with transfusion and RCI lab
2. Transfuse if life threatening
3. Complement inhibitors show promise for management of autoimmune haemolytic anaemias
4. Other treatment modalities coming through

Thank you for your attention

